CLAIMS

What is claimed is:

1. A method for determining the genotype at the site of a polymorphism in a target polynucleotide sequence comprising:

a. contacting a first partial duplex comprising a target polynucleotide sequence with a second partial duplex comprising a mutated reference polynucleotide sequence under conditions in which said first and said second partial duplexes form a four-way complex, wherein said mutated reference polynucleotide is identical to a reference polynucleotide everywhere except at the site of a mutation that is not at the site of the polymorphism, and wherein said reference polynucleotide sequence corresponds to said target polynucleotide sequence and has a known genotype at the site of the polymorphism;

b. subjecting said four-way complex to branch migration conditions, wherein branch migration in said four-way complex is impeded at or near the site of the polymorphism if the target polynucleotide sequence has a genotype at the site of the polymorphism that differs from that of the reference polynucleotide sequence, thereby forming a stabilized four-way complex, and wherein branch migration in the four-way complex is capable of continuing until complete strand exchange occurs if the target polynucleotide sequence and the reference polynucleotide sequence share the same genotype at the site of the polymorphism, thereby resulting in the resolution of said four-way complex into two duplex nucleic acids; and

c. detecting said stabilized four-way complex as an indication that said target polynucleotide sequence has a genotype that is different from the known genotype of said reference polynucleotide sequence at said site of the polymorphism, or detecting resolution of said four-way complex as an indication that said target polynucleotide sequence has a genotype that is the same as the known genotype of

said reference polynucleotide sequence at said site of the polymorphism.

2. The method of Claim 1, wherein said mutated reference polynucleotide sequence and said target polynucleotide sequence differ at the site of the mutation.

3. The method of Claim 2, wherein said mutation is a single-base mutation.

4. The method of Claim 2, wherein said mutation is a multiple-base mutation or a mutation that comprises multiple single-base mutations.

5. The method of Claim 1, wherein said mutation is less than 20 nucleotides away from said site of the polymorphism.

6. The method of Claim 5, wherein said mutation is 4, 3, or 2 nucleotides away from said site of the polymorphism or adjacent to the site of the polymorphism.

7. The method of Claim 6, wherein said mutation is 5' of said site of the polymorphism and adjacent to said site of the polymorphism.

8. The method of Claim 6, wherein said mutation is 3' of said site of the polymorphism and adjacent to said site of the polymorphism.

9. The method of Claim 1, wherein said first and said second partial duplexes comprise GC-rich sequences.

10. The method of Claim 1, wherein said first and said second partial duplexes comprise minor groove binding motifs.

11. The method of Claim 1, wherein said first and second partial duplexes comprise nucleic acid modifications or peptide nucleic acid backbones.

12. A method for determining the genotype at the site of a polymorphism in a target polynucleotide sequence comprising:

a. contacting a first partial duplex comprising a mutated target polynucleotide sequence with a second partial duplex comprising a reference polynucleotide sequence, wherein said mutated target polynucleotide sequence is identical to a target polynucleotide sequence everywhere except at the site of a mutation that is not at the site of the polymorphism, and wherein said reference polynucleotide sequence corresponds to said target polynucleotide sequence and has a known genotype at the site of the polymorphism;

b. subjecting said four-way complex to branch migration conditions, wherein branch migration in said four-way complex is impeded at or near the site of the polymorphism if the target polynucleotide sequence has a genotype at the site of the polymorphism that differs from that of the reference polynucleotide sequence, thereby forming a stabilized four-way complex, and wherein branch migration in the four-way complex is capable of continuing until complete strand exchange occurs if the target polynucleotide sequence and the reference polynucleotide sequence share the same genotype at the site of the polymorphism, thereby resulting in the resolution of said four-way complex into two duplex nucleic acids; and

c. detecting said stabilized four-way complex as an indication that said target polynucleotide sequence has a genotype that is different from the known genotype of said reference polynucleotide sequence at said site of the polymorphism, or detecting resolution of said four-way complex as an indication that said target polynucleotide sequence has a genotype that is the same as the known genotype of said reference polynucleotide sequence at said site of the polymorphism.

13. The method of Claim 12, wherein said mutated target polynucleotide sequence and said reference polynucleotide sequence differ at the site of the mutation.

14. The method of Claim 13, wherein said mutation is a single-base mutation.

15. The method of Claim 13, wherein said mutation is a multiple-base mutation or a mutation that comprises multiple single-base mutations.

16. The method of Claim 13, wherein said mutation is less than 20 nucleotides away from said site of the polymorphism.

17. The method of Claim 16, wherein said mutation is 4, 3, or 2 nucleotides away from said site of the polymorphism or adjacent to said site of the polymorphism.

18. The method of Claim 17, wherein said mutation is 5' of said site of the polymorphism and adjacent to said site of the polymorphism.

19. The method of Claim 17, wherein said mutation is 3' of said site of the polymorphism and adjacent to said site of the polymorphism.

20. The method of Claim 12, wherein said first and said second partial duplexes comprise GC-rich sequences.

21. The method of Claim 12, wherein said first and said second partial duplexes comprise minor groove binding motifs.

22. The method of Claim 12, wherein said first and said second partial duplexes comprise nucleic acid modifications or peptide nucleic acid backbones.

23. A method for determining the genotype at the site of a polymorphism in a target polynucleotide sequence comprising:

a. contacting a first partial duplex comprising a mutated target polynucleotide sequence with a second partial duplex comprising a mutated reference

polynucleotide sequence having a known genotype at the site of the polymorphism under conditions in which said first and said second partial duplexes form a four-way complex, wherein said mutated target polynucleotide sequence is identical to a target polynucleotide sequence everywhere except at the site of a mutation that is not at the site of the polymorphism, wherein said mutated reference polynucleotide is identical to a reference polynucleotide everywhere except at the site of a mutation that is not at the site of the polymorphism, and wherein said reference polynucleotide sequence corresponds to said target polynucleotide sequence and has a known genotype at the site of the polymorphism;

b. subjecting said four-way complex to branch migration conditions, wherein branch migration in said four-way complex is impeded at or near the site of the polymorphism if the target polynucleotide sequence has a genotype at the site of the polymorphism that differs from that of the reference polynucleotide sequence, thereby forming a stabilized four-way complex, and wherein branch migration in the four-way complex is capable of continuing until complete strand exchange occurs if the target polynucleotide sequence and the reference polynucleotide sequence share the same genotype at the site of the polymorphism, thereby resulting in the resolution of said four-way complex into two duplex nucleic acids; and

c. detecting said stabilized four-way complex as an indication that said target polynucleotide sequence has a genotype that is different from the known genotype of said reference polynucleotide sequence at said site of the polymorphism, or detecting resolution of said four-way complex as an indication that said target polynucleotide sequence has a genotype that is the same as the known genotype of said reference polynucleotide sequence at said site of the polymorphism.

24. The method of Claim 12, wherein said mutated target polynucleotide sequence and said mutated reference polynucleotide sequence differ at the site of said first mutation or said second mutation.

25. A method for determining the genotype at the site of a polymorphism in a target polynucleotide sequence comprising:

a. contacting a first partial duplex comprising a target polynucleotide sequence with a second partial duplex comprising a reference polynucleotide sequence having a known genotype at the site of the polymorphism under conditions in which said first and said second partial duplexes form a four-way complex, and wherein said first and said second partial duplex each comprise a nucleic acid modification;

b. subjecting said four-way complex to branch migration conditions, wherein branch migration in said four-way complex is impeded at or near the site of the polymorphism if the target polynucleotide sequence has a genotype at the site of the polymorphism that differs from that of the reference polynucleotide sequence, thereby forming a stabilized four-way complex, and wherein branch migration in the four-way complex is capable of continuing until complete strand exchange occurs if the target polynucleotide sequence and the reference polynucleotide sequence share the same genotype at the site of the polymorphism, thereby resulting in the resolution of said four-way complex into two duplex nucleic acids; and

c. detecting said stabilized four-way complex as an indication that said target polynucleotide sequence has a genotype that is different from the known genotype of said reference polynucleotide sequence at said site of the polymorphism, or detecting resolution of said four-way complex as an indication that said target polynucleotide sequence has a genotype that is the same as the known genotype of said reference polynucleotide sequence at said site of the polymorphism.

26. The method of Claim 25, wherein said nucleic acid modification is a GC clamp, a minor groove binding motif, a nucleic acid backbone modification or a peptide nucleic acid backbone.